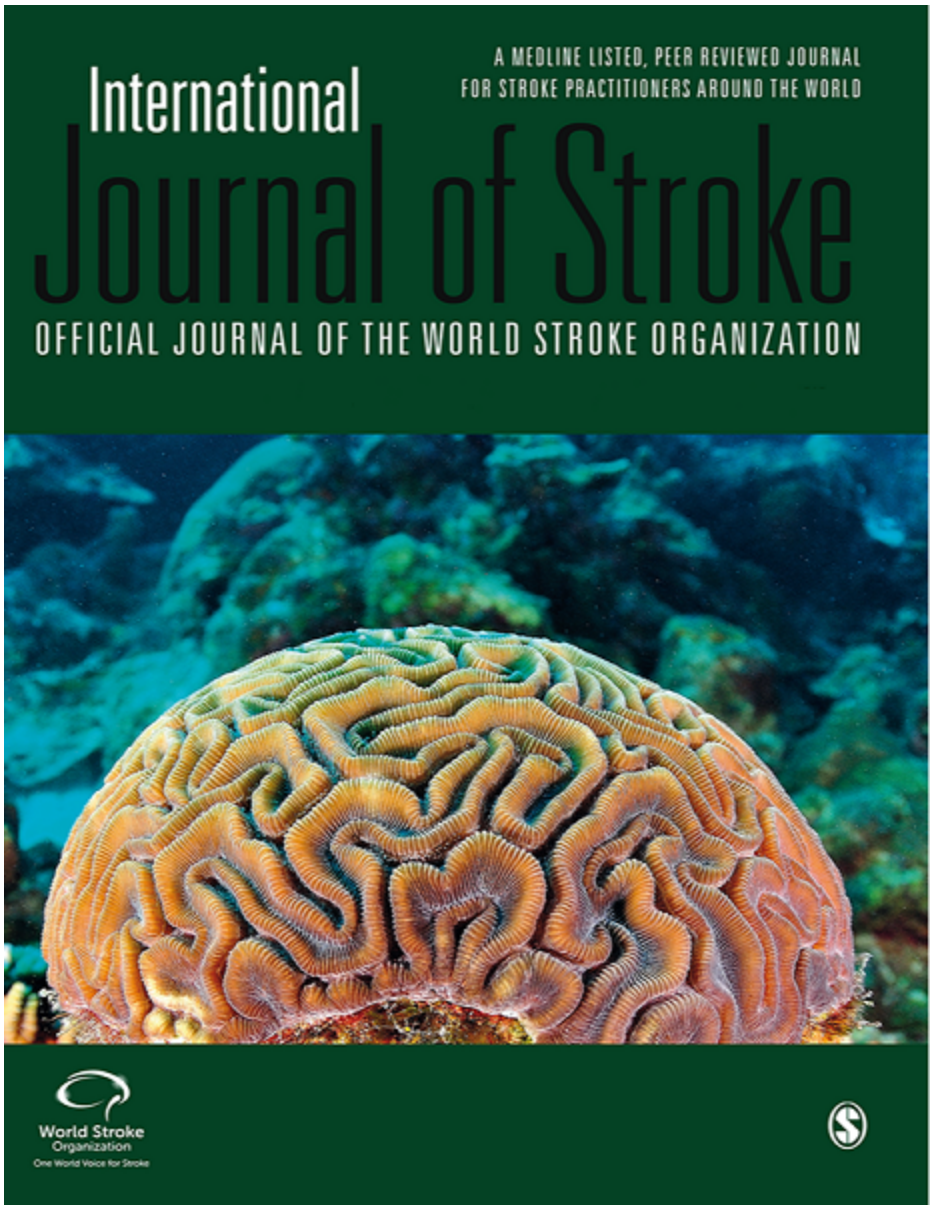

Total Mismatch in Diffusion Negative Patients in the WAKE-UP Trial

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Total Mismatch in Diffusion Negative Patients in the WAKE-UP Trial

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Dear Editor,

The WAKE-UP trial screened patients in the unknown time window after stroke onset for the presence of a DWI-FLAIR mismatch [1]. Since perfusion-weighted imaging (PWI) was not mandatory, the pattern of a total mismatch, i.e. a negative DWI together with a positive PWI lesion, remained undetected in the primary analysis [2-6].

In a post-hoc analysis, we investigated the incidence of the total mismatch profile in patients enrolled in the WAKE-UP trial. For patients with available PWI, we calculated DWI and PWI lesion volumes with RAPID (iSchemaView, Menlo Park, CA). Of 1,362 patients enrolled, PWI was available in 343 (25%). Of these, only 3 (0.9%) had a total mismatch caused by a M2 occlusion of the middle cerebral artery (Figure 1).

Figure 1. DWI and PWI analysis in total mismatch patients

[Insert figure 1.]

DWI (A), PWI lesion with a time to maximum of the residue function (Tmax) >6s (B), PWI lesions with different Tmax value (C) generated by RAPID software (iSchemaView) and time-of-flight magnetic resonance angiography (D). For patient 1, 2 and 3, time from symptom recognition to imaging was 80, 269 and 90 min, time from last seen well to imaging was 410, 899 and 510 min and PWI lesion volume was 70, 76 and 32 ml respectively. All patients had an M2 occlusion of the left middle cerebral artery.

Less than one percent of patients had a total mismatch. The absence of a DWI lesion in patients presenting with stroke-like symptoms should prompt the clinician to consider stroke mimics. Additional PWI can guide physicians to determine a vascular etiology for the neurological symptoms, which can be confirmed by identifying a vessel occlusion on magnetic resonance

angiography. Apart from stroke mimics, early imaging after stroke onset, stroke in the posterior circulation and stroke caused by small vessel disease can all lead to DWI negativity.[7] None of these were present in the 3 total mismatch patients. The confirmation of a vessel occlusion excluded early (partial) reperfusion as a possible explanation for DWI negativity.

Since randomization in the WAKE-UP trial was based on the presence of the DWI-FLAIR mismatch [1], these patients were not randomized and assigned to a particular treatment arm. Given the infinite PWI-DWI mismatch ratio, they might have been ideal candidates for reperfusion treatment. The natural course and benefit from treatment in these patients is not well known. Withholding reperfusion treatment might therefore be hazardous as long as the fate of the hypoperfused tissue remains uncertain. [2-6]

When evaluating patients for the DWI-FLAIR mismatch, PWI can provide additional information to ensure the most comprehensive patient selection, although the total mismatch pattern may be uncommon.

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Conflicts-of-Interest/disclosures

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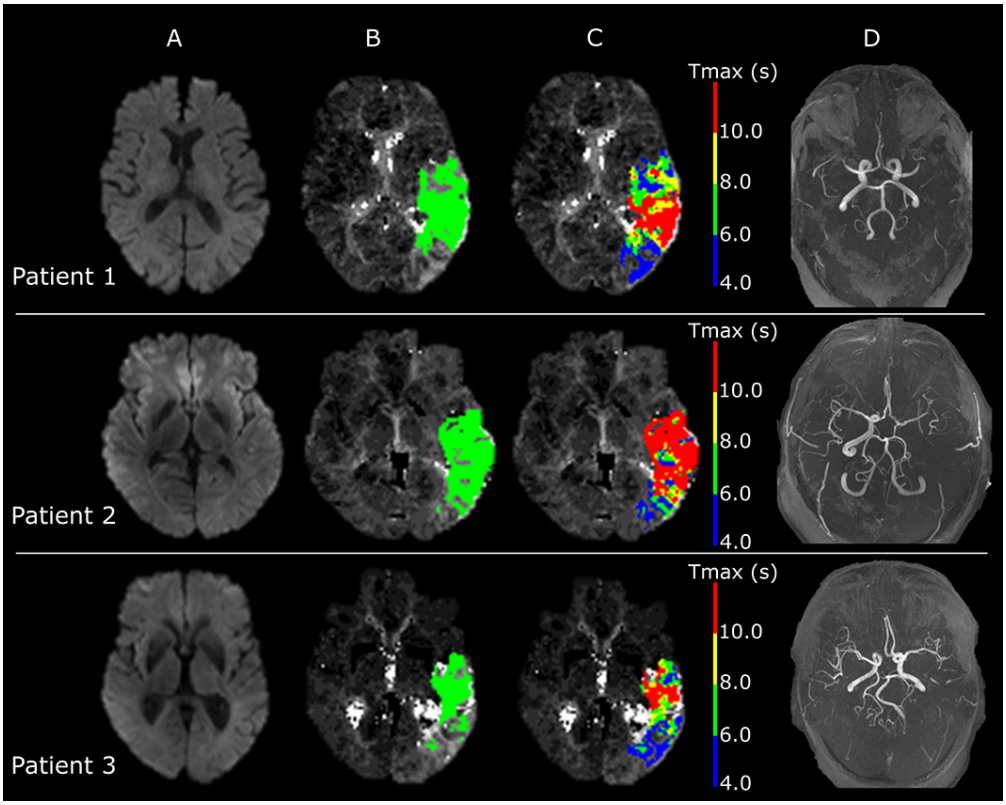

DWI (A), PWI lesion with a time to maximum of the residue function (Tmax) >6s (B), PWI lesions with different Tmax value (C) generated by RAPID software (iSchemaView) and time-of-flight magnetic resonance angiography (D). For patient 1, 2 and 3, time from symptom recognition to imaging was 80, 269 and 90 min, time from last seen well to imaging was 410, 899 and 510 min and PWI lesion volume was 70, 76 and 32 ml respectively. All patients had an M2 occlusion of the left middle cerebral artery.